Prediction of Difficult Laryngoscopy Using Ultrasound: A Systematic Review and Meta-Analysis

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OBJECTIVES: Evaluate associations between ultrasound measures and difficult laryngoscopy.

DATA SOURCES: MEDLINE, Embase, Google Scholar, Web of Science, and the Cochrane Library were searched using MeSH terms and keywords.

STUDY SELECTION: Studies published in English describing the use of airway ultrasound for identifying difficult laryngoscopy, with sufficient data to calculate sensitivity and specificity using 2 × 2 tables.

DATA EXTRACTION: We assigned the described indices of airway dimension to one of three domains based on methodology characteristics: anterior tissue thickness domain, anatomical position domain, and oral space domain. We then performed a bivariate random-effects meta-analysis, deriving pooled sensitivity, specificity, diagnostic odds ratio, positive likelihood ratio, and negative likelihood ratio estimates. We assessed risks of bias using Quality Assessment of Diagnostic Accuracy Studies-2 analysis.

DATA SYNTHESIS: Thirty-three studies evaluating 27 unique indices were included in the meta-analysis. The ultrasound protocols of the included studies were heterogeneous. Anterior tissue thickness demonstrated a pooled sensitivity of 76% (95% CI, 71–81%), specificity of 77% (95% CI, 72–81%), and an area under the receiver operating characteristic curve (AUROC) of 0.83 (95% CI, 0.80–0.86). Anatomical position demonstrated a pooled sensitivity of 74% (95% CI, 61–84%), specificity of 86% (95% CI, 78–91%), and an AUROC of 0.87 (95% CI, 0.84–0.90). Oral space demonstrated a pooled sensitivity of 53% (95% CI, 0.36–0.69), specificity of 77% (95% CI, 0.67–0.85), and an AUROC of 0.73 (95% CI, 0.69–0.77).

CONCLUSIONS: Airway ultrasound metrics associate with difficult laryngoscopy in three domains: anterior tissue thickness, anatomic position, and oral space. An assessment instrument combining clinical and ultrasound assessments may be an accurate screening tool for difficult laryngoscopy.

KEY WORDS: Cormack-Lehane; difficult airway; hyomental distance; intubation; point-of-care ultrasound (POCUS); quality and safety

Difficult intubation affects between 4.5% and 7.5% of operating room cases and is a critical event in perioperative management (1, 2). Predicting difficult intubation is challenging in patients with unknown airway morphology, especially in emergencies or in cases where patients are unstable. Early identification of risks for difficult intubation decreases the potential for catastrophic events (3, 4).

Physical examination is traditionally the principal means for predicting difficult intubation (2). Typical assessments include the modified Mallampati score (sensitivity 53%, specificity 80%), the upper lip bite test (sensitivity 67%, specificity

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DOI: 10.1097/CCM.0000000000005711

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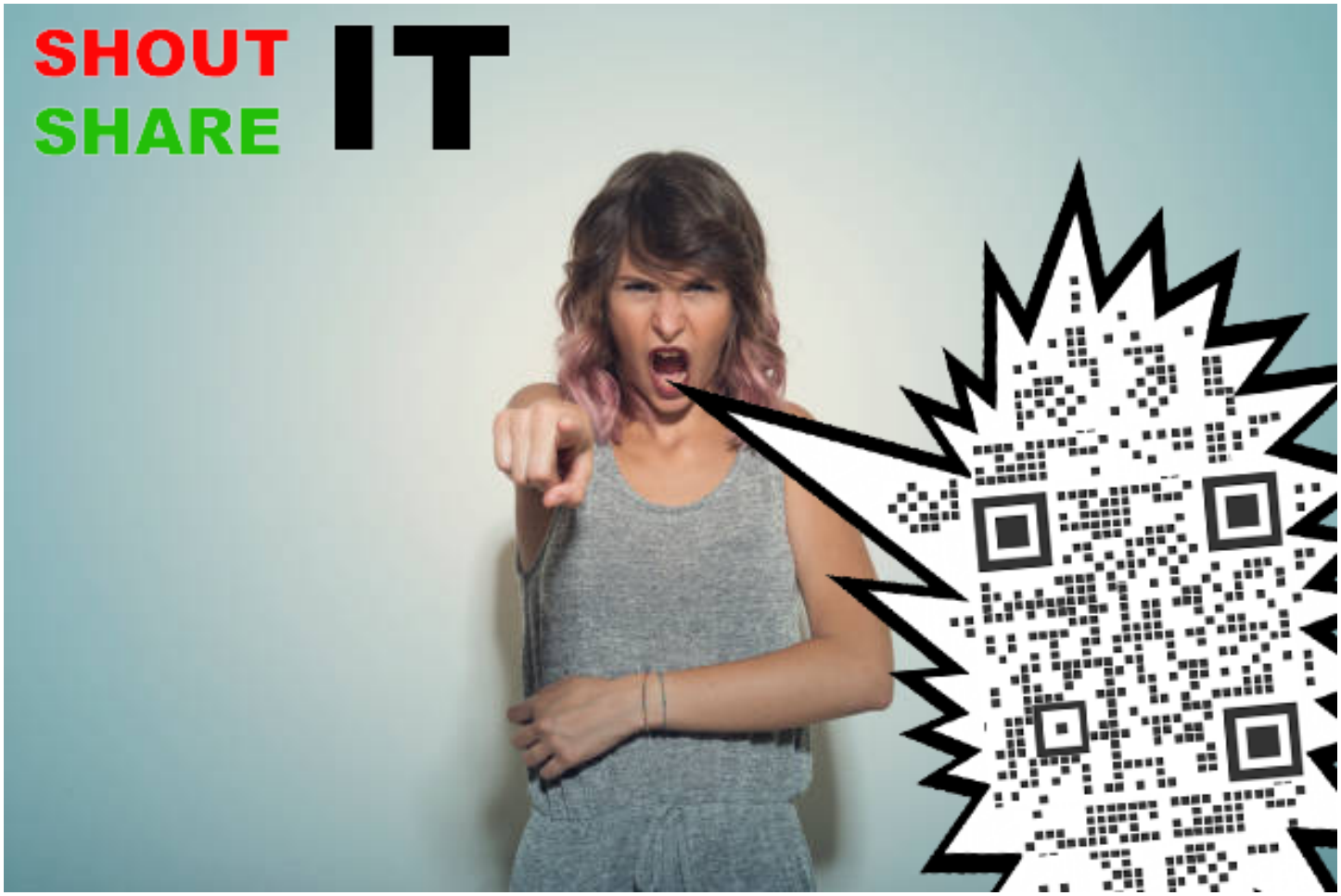
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KEY POINTS

Question: Can airway evaluation using ultrasound accurately predict difficult laryngoscopy?

Findings: This systematic review combined airway evaluation ultrasound indices into three assessment domains. Indices in the anatomical position domain performed the best, with an area under the receiver operating characteristic curve (AUROC) of 0.87 (95% CI, 0.84–0.90) compared with the tissue thickness domain and the oral space domain, with AUROCs of 0.83 (95% CI, 0.80–0.86) and 0.73 (95% CI, 0.69–0.77), respectively. A three-component ultrasound assessment using a test from each domain is potentially more predictive for difficult laryngoscopy.

Meaning: An assessment instrument combining ultrasound assessments is likely more meaningful than single tests in screening for difficult laryngoscopy.

92%), and the thyromental distance (sensitivity 37%, specificity 89%) (5). These assessments have low to moderate sensitivity and moderate to fair specificity, limiting their utility as independent screening tests (2). Authors have described several composite airway scoring systems for improving the identification of difficult intubation. These systems apply multiple assessments toward scoring risk for difficult intubation and include the Simplified Predictive Intubation Difficulty Score (6) and the Total Airway Score (7), among others. However, the performances of these composite measures are not appreciably better than physical examination, with sensitivities below 0.69 (6, 7).

Ultrasound is widely available in critical care, perioperative, and emergency settings where intubation is likely. Rapid ultrasound assessments may identify difficult laryngoscopy, with an increasing number of studies evaluating ultrasound estimates of anterior neck soft-tissue thickness, oral cavity space, anatomic mobility, and laryngeal position. As an example, Petrişor et al (8) measured the distance between the hyoid bone and the mentum as a predictor of difficult laryngoscopy (**Supplemental Fig. 1**, (http://links.lww.com/CCM/H237). Ultrasound assessment is noninvasive and often readily tolerated by patients. It also safely provides the dimensions of oropharyngeal and tracheal structures that otherwise require invasive endoscopy or radiographic imaging. Ultrasound can also provide biometric data that are precise to within fractions of a millimeter, presenting unique opportunities for measuring relevant pathology in difficult airways.

Previous systematic reviews and meta-analyses have pooled multiple ultrasound measures for identifying difficult laryngoscopy without subcategorizing them by their methodological similarities (9–12). These reviews not only noted potential utility for ultrasound airway assessment but also noted large heterogeneity in study methodology, measurement thresholds, and population groups. These heterogeneities limit users from drawing conclusions about ultrasound's utility in identifying difficult airways, and methodology standardization is needed. Conceptually, ultrasound measures in published studies are categorizable into three major domains: tests of "anterior neck tissue thickness," dynamic tests related to "anatomic position changes" relevant during intubation, and tests indicating potential "oral cavity space." These metrics are analogous to physical examination indicators of the potential difficult airway, such as estimates of jaw and neck excursion, mouth opening, and oropharyngeal space. Ultrasound provides a quantifiable, noninvasive means of measuring these relevant indicators before induction. A domain-based analysis of the airway ultrasound literature on difficult laryngoscopy has not been previously published.

The objective of this systematic review was a comprehensive evaluation of the published literature on airway ultrasound assessments for identifying difficult laryngoscopy, and meta-analyses of these assessments pooled into three major domains defined as anterior neck tissue thickness, anatomic position changes, and oral cavity space measures.

MATERIALS AND METHODS

This systematic review and meta-analysis was performed in accordance with the Cochrane Handbook for Systematic Reviews of Interventions and reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (9). The University of Alabama Institutional Review Board (IRB) waived the need for IRB approval.

Search Strategy

MEDLINE, Embase, Google Scholar, Web of Science, and the Cochrane Library were searched using MeSH terms and keywords selected by a literature review. All

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abstracts available by June 30, 2021, were included in the search strategy. The search strategy for all databases specified is attached (**Supplemental Content**, http://links.lww.com/CCM/H237). The references of included articles and previously performed meta-analyses were also searched and screened for inclusion in this systematic review and meta-analysis.

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Study Selection and Data Extraction

Clinical trials or observational studies (retrospective or prospective) examining associations between ultrasound assessments and difficult intubation and/or difficult laryngoscopy were included. Studies not written in the English language were excluded. Studies were excluded if 2 × 2 tables for the derivation of sensitivity and specificity were not calculable. In studies where 2 × 2 table data were not directly presented, the tables were derived from accuracy, disease prevalence, and sample size measures. Authors were contacted if these data were not available. Case reports, case series of fewer than 10 cases, reviews, abstracts, editorials, and other meta-analyses on the subject were excluded. Study selection and screening were managed with systematic literature review software (Covidence, Veritas Health Innovation, Melbourne, VIC, Australia; www.covidence.org). Abstracts were independently screened by two reviewers (V.B., N.A.R.). The senior author (E.S) adjudicated disagreements. The screened abstracts were then selected for full-text citations (V.B., N.A.R.). The senior author (E.S.) resolved disagreements. Two reviewers (V.B., N.A.R.) independently extracted data regarding study populations, methodology, results, and characteristics relevant for bias assessment. We used the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) statement to assess applicability and risk of bias (7).

Outcomes

The primary outcome was difficult laryngoscopy, using either the Cormack-Lehane Classification or difficult intubation as a gold standard. The ultrasound tests were divided into one of the three domains based on their methodology. The three domains were as follows: 1) ultrasound tests evaluating anterior neck soft-tissue thickness (tissue thickness domain [TTD]), 2) ultrasound tests evaluating the dynamic motion of the neck or tongue or position of the hyoid bone to the mentum (anatomical position domain [APD]), and 3) ultrasound tests evaluating for space in the floor of mouth such as the size of the tongue (oral space domain [OSD]). Secondary objectives included evaluating the quality and limitations of existing studies on the topic.

Data Synthesis and Analysis

A bivariate random-effects meta-analysis was performed using the pooled true and false positive and negative data from each study, deriving pooled sensitivity, specificity, diagnostic odds ratio, positive likelihood ratio, and negative likelihood ratio estimates. This bivariate approach explicitly incorporates the negative correlation between sensitivity and specificity into the analysis, in line with prior meta-analyses (8, 9). We evaluated publication bias using Deek's funnel plot asymmetry test and report study heterogeneity using I^2. Meta-analysis results are graphically depicted using receiver operating characteristic (ROC) plots, forest plots, and Fagan nomograms (using the observed disease prevalence as the prior probability). A separate bivariate random-effects meta-analysis was performed for all ultrasound measures under each of the three domains. If a study evaluated more than one ultrasound test, its data were used once for each relevant domain in assessing diagnostic accuracy. However, in the weighting of the studies, each patient was only counted once, avoiding misanalysing multiple observations as multiple patients. We performed subgroup analyses evaluating differences in pooled diagnostic accuracy measures in the three domains based on the prevalence of difficult laryngoscopy. Statistical analysis software packages (R Core Team, Vienna, Austria; Stata 15.0, StataCorp, LLC, College Station, TX) were used to perform the meta-analysis. A p value of less than 0.05 was considered statistically significant.

RESULTS

The initial search returned 639 results. After removing duplicates and screening for abstracts that did not meet inclusion criteria, 61 abstracts were selected for full-text review. Thirty studies were excluded for reasons described in the PRISMA flow diagram (**Fig. 1**). Two additional studies were included after a review of references of the articles (6, 13).

Thirty-three studies with 8,409 adult patients were included in the meta-analysis. All included studies were prospective observational cohort studies of patients

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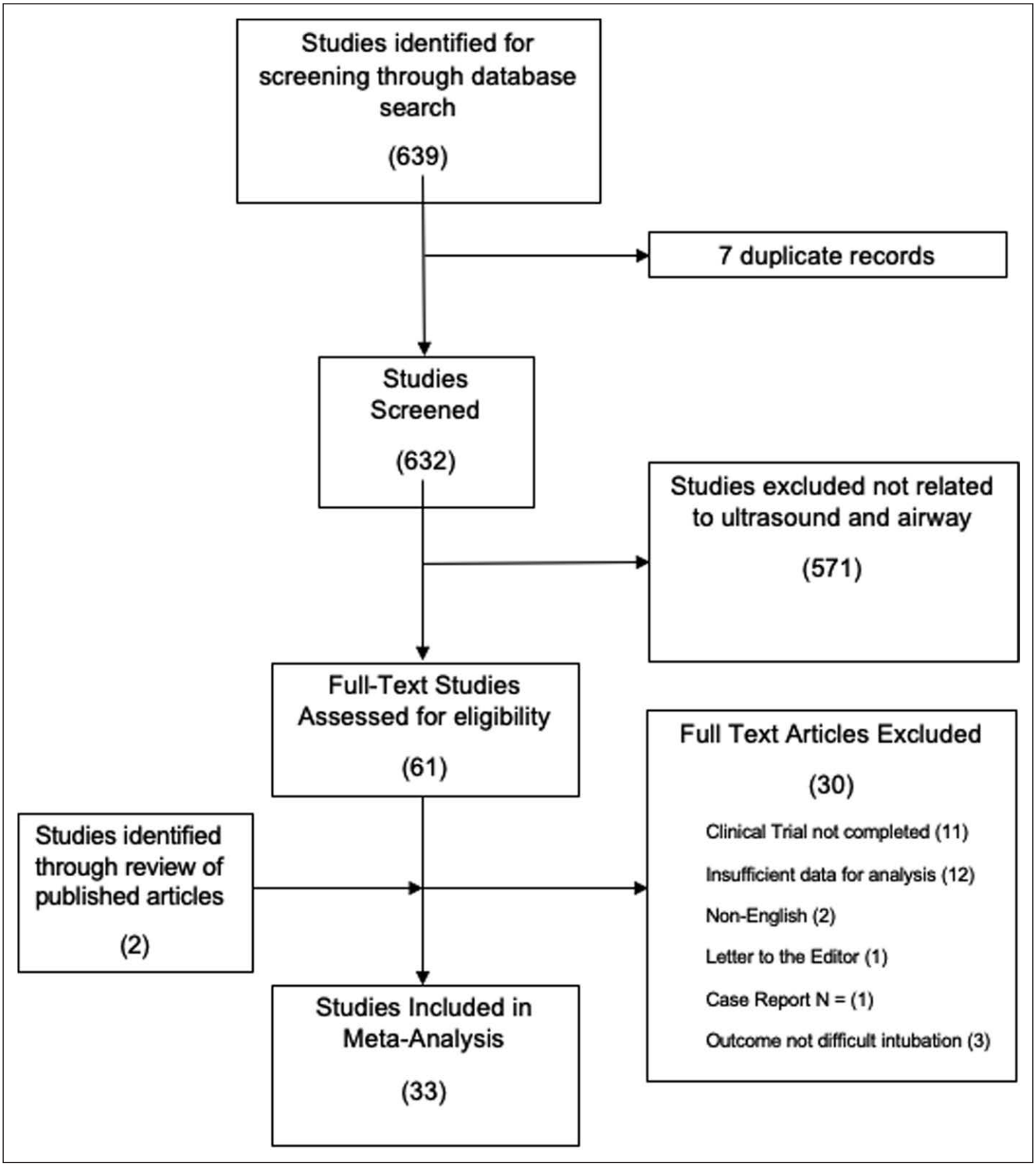

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram for study selection for systematic review.

undergoing airway assessment for endotracheal intubation in elective surgical procedures. There were 27 unique ultrasound measures evaluated in the included studies. Full study characteristics are described in **Supplemental Table 1** (http://links.lww.com/CCM/H237). The prevalence of difficult laryngoscopy ranged from 4% to 38.33% in individual studies (7, 14), with an overall prevalence of 9%.

Patients with known difficult airways or the presence of features likely associated with difficult airways were excluded by most studies (6, 13–25). However,

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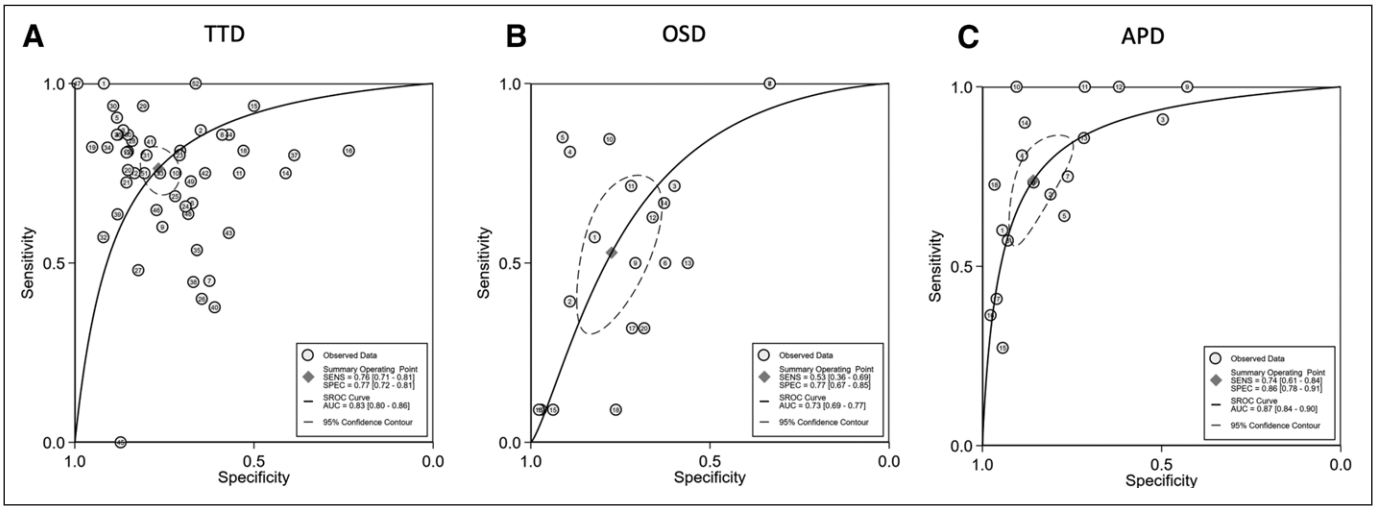

Figure 2. A, Hierarchical summary receiver operating characteristic (HSROC) curve for all estimates evaluating anterior neck soft-tissue thickness (tissue thickness domain [TTD]). **B**, HSROC curve for all estimates evaluating oropharyngeal space (OSD). **C**, HSROC curve for all estimates evaluating neck position and tongue displacement (anatomical position domain [APD]). Studies inside the olive have narrow CI and a high degree of reliability. AUC = area under the curve, SENS = sensitivity, SPEC = specificity, SROC = summary receiver operating characteristic.

half of the studies did not mention the exclusion of known difficult airway patients (7, 26–39). All but three studies excluded morbidly obese patients (25, 8, 33). Several studies excluded pregnant patients (7, 14, 15, 23, 34–36), whereas Xu et al (37) focused exclusively on pregnant patients.

Ultrasound training and experience were not defined in multiple studies (6, 13, 13, 14, 18, 21, 23–28, 31–33, 35–39). Ultrasound was performed by clinicians with quantifiable experience in three studies (15, 19, 20), and the remaining studies only described the sonographers as having received training or experience (7, 13, 16, 17, 22, 29, 30, 34, 40–42). Two studies performed the ultrasound airway assessment postoperatively (16, 18).

Thresholds for identifying difficult laryngoscopy varied widely across the studies, even among methodologically similar ultrasound assessments. Actual difficult intubation was used as a comparator to ultrasound methods in three studies (15, 18, 42), and versions of the Cormack-Lehane classification were the reference standard in the remaining studies. When mentioned, the Cormack-Lehane classification was performed by anesthesiologists with 2–10 years of experience in studies (6, 8, 13, 15–18, 21, 23, 25, 26, 28–34, 36, 38, 40, 42), but relevant experience was not described in nine studies (7, 14, 18, 19, 23, 26, 35, 39).

Ultrasound variables assessed in each study were grouped into three domains based on their relevance to assessing anterior neck soft-tissue thickness (TTD), anatomic positioning concerns (APD), or oral space (OSD) (**Supplemental Table 2**, http://links.lww.com/CCM/H237). The pooled sensitivity and specificity for each domain were calculated, with APD demonstrating an area under the ROC of 0.87 (pooled sensitivity of 74% and specificity of 86%), compared with 0.83 in the TTD (sensitivity 76%, specificity 77%) and 0.73 in the OSD (53% sensitivity, 77% specificity) (**Table 1** and **Fig. 2**). A forest plot was created for each domain (**Supplemental Fig. 2**, http://links.lww.com/CCM/H237).

Deek's funnel plot asymmetry test did not identify publication bias across subgroups (TTD $p = 0.97$, APD $p = 0.94$, OSD $p = 0.51$) (**Supplemental Fig. 3**, http://links.lww.com/CCM/H237). The risk of bias was judged as low with the use of the Cormack-Lehane classification and difficult intubation as the reference tests and also judged as low with the index ultrasound tests. The overall risk of bias in patient selection was judged as low in all but one study where it was unclear (6). The risk of bias was unclear in two studies in the domains of index test and reference test (6, 13); blinding status was not reported in both studies. In several studies, risk of bias was unclear in the timing of ultrasound and result reporting (14, 19, 26, 39, 40). Concerns of applicability in a general population were judged as high in three studies: Jain et al (24) and Petrişor et al (31) only evaluated patients with morbid obesity, and

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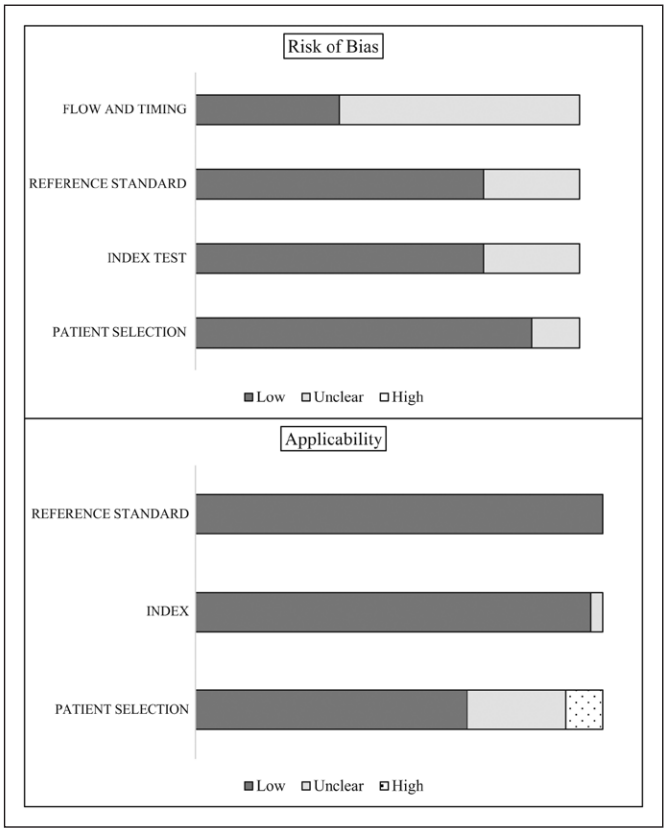

Figure 3. A histogram depicting Quality Assessment of Diagnostic Accuracy Studies-2 analysis for evaluating the risk of bias and applicability for all studies included in the meta-analysis. The first histogram shows the risk of bias, and the second histogram depicts the applicability of the studies.

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Xu et al (37) evaluated pregnant patients. Applicability was unclear in seven studies that excluded obese and/or pregnant patients (20, 22, 23, 31, 34, 35, 38) (**Fig. 3**; and **Supplemental Table 3**, http://links.lww.com/CCM/H237).

DISCUSSION

This is the first systematic review and meta-analysis of ultrasound as an assessment tool for potential difficult laryngoscopy that examines airway ultrasound measurements within methodologically related domains. This approach aggregates analyses of related variables and facilitates the development of standardized approaches for ultrasound airway assessment. This systematic review is the most extensive one on this topic, including 8,409 patients from 33 studies. Measures assessing anatomical positioning (APD) performed best in terms of sensitivity and specificity among the three domains. Independently, these pooled sensitivities slightly outperform physical examination-based assessments and scoring systems for predicting difficult laryngoscopy.

The TTD indices estimated the soft-tissue thickness at the level of several anatomical structures such as the epiglottis, larynx, and hyoid bone. These indices provide information on the volume and compliance of the submandibular space that in turn affects the curvature of the path the laryngoscope must take for orotracheal intubation (43). Even though thresholds used for identifying difficult laryngoscopy varied among the studies, the pooled sensitivity and specificity were acceptable. Similar associations between difficult laryngoscopy and anterior neck tissue thicknesses in front of the hyoid bone, epiglottis, and anterior commissure of vocal cords have been described in published literature (44).

Ultrasound measurements in the APD domain included measurements of the angle between the glottis and the epiglottis (29), condylar translation (37), and the ratio of hyomental distance measured in neutral and extended neck positions (16, 28, 31–33, 39). These measurements estimate the range of atlantooccipital extension or tongue displacement with head positioning for glottic visualization. Measurements in the APD domain allow static and dynamic assessment of mobility and position-dependence that can influence safe intubation (15, 16, 21).

The OSD tests evaluated whether limitations on oropharyngeal space could restrict laryngoscopy, as a small oral cavity directly impairs visualization as well as instrumentation of the airway. The sensitivity and specificity of individual tests were lower for most of the studies in this domain in comparison with TTD and APD assessments. Two of these studies' authors commented that OSD tests demonstrate limited accuracy (16, 23). A potential reason could be that ultrasound cannot adequately visualize the dimensions of an air-filled oropharynx irrespective of the size of the tongue and other soft tissues adjacent to it.

Heterogeneity among the studies is well described (44–48) and has hindered generalizing data on the efficacy of airway ultrasound. Heterogeneity exists in the available literature regarding patients, equipment, measurements, and thresholds among varying tests for predicting difficult laryngoscopy. Examining the airway ultrasound tests in their respective domains provides information on the comparative accuracy of different methodological

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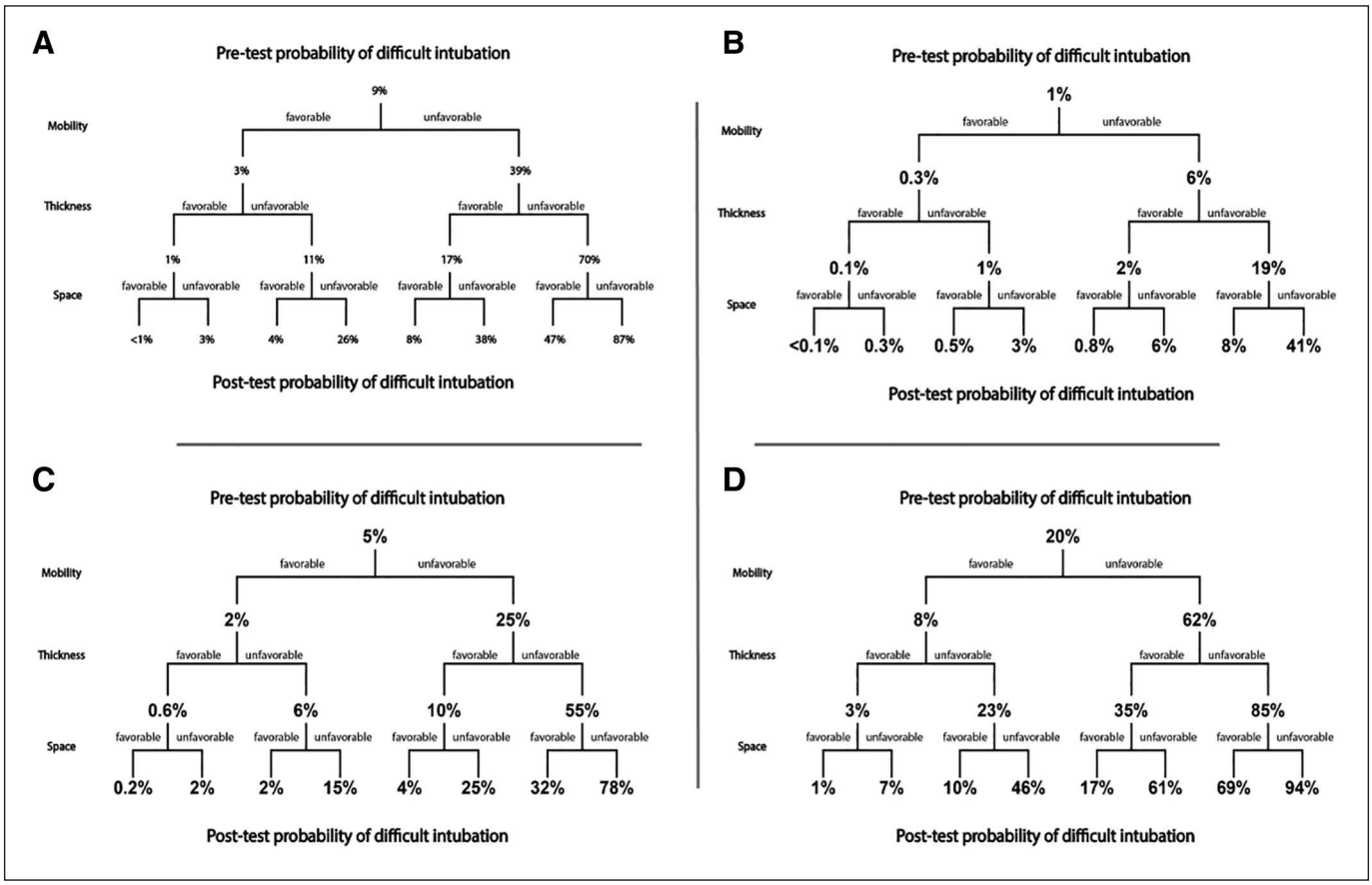

Figure 4. A hypothetical flow chart depicting the utility of multiple ultrasound tests in succession. A favorable test suggests a higher likelihood for an easy laryngoscopy, and an unfavorable examination suggests a higher likelihood for a difficult laryngoscopy. Different combinations of favorable and unfavorable tests are presented toward computing a posttest probability. A pretest probability of 9% (**A**) is the pooled prevalence of difficult laryngoscopy from all the included studies. Hypothetical pre-test probabilities of 1% (**B**), 5% (**C**), and 20% (**D**) are also presented.

approaches. However, as seen in these analyses, the sensitivity of airway ultrasound tests within each domain is moderate, and specificity is moderate to fair. Each of the three airway ultrasound assessment domains only demonstrates a marginal benefit over traditional physical examination assessment for difficult laryngoscopy.

If the modalities are integrated like other multifactor outcome risk assessment tools such as Acute Physiology and Chronic Health Evaluation-II, a more granular risk assessment is possible (**Fig. 4**) and potentially superior to individual tests. For example (**Fig. 4*A***), if one presumes a pooled pretest probability of 9% for difficult laryngoscopy as derived from this meta-analysis, an APD ultrasound assessment that does not suggest difficult laryngoscopy decreases its probability to an estimate of 3%. Using this 3% as the pretest probability for TTD ultrasound, a reassuring assessment further reduces the likelihood of difficult laryngoscopy to 1%. Finally, presuming a pretest probability of 1% for difficult laryngoscopy, an OSD ultrasound assessment that is reassuring can reduce its posttest probability to less than 1%. Conversely, results suggesting difficult laryngoscopy in all three domains suggest a cumulative probability of 87%. The probability decreases to 70% when two of three domains suggest difficult laryngoscopy and to 39% when only one test in one domain predicts difficult laryngoscopy. These respective posttest probabilities would differ in populations with lower or higher pretest probability of difficult laryngoscopy. This is further exemplified in **Figure 4B–*D*** using pretest probabilities of 1%, 5%, and 20%. The projections are merely estimates, and prospective testing of a clearly defined protocol is necessary for understanding the true diagnostic potential of this approach. In contrast to previously published meta-analyses, these estimates may suggest the benefit of a multimodal assessment of different parts of the airway.

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Limitations to this review include that most of the studies compared airway ultrasound with versions of the Cormack-Lehane classification, which is itself an assessment of difficult laryngoscopy and not necessarily equivalent to difficult intubation. The Cormack-Lehane classification was first described in 1984 (49, 50) and is an established standard for characterizing difficult laryngoscopy as a risk for difficult intubation based on the appearance of the oropharynx under laryngoscopy. However, it may have interpretation issues, as one survey of 120 anesthesia providers demonstrated only fair interobserver agreement, with 75% of respondents not describing grades correctly (51). Koh et al (52) described a seminal prospective observational study of 605 patients receiving endotracheal intubation for elective surgery. In this study, 5.1% of patients demonstrated an unfavorable modified Cormack-Lehane Grade of 2b or greater, with 71% of these patients experiencing difficult intubation. Similarly, in another prospective study by Yentis et al (50), 663 patients requiring endotracheal intubation for elective surgery were evaluated, and 7.6% had an unfavorable modified Cormack-Lehane Grade. Among these patients with unfavorable Cormack-Lehane grading, 70.5% experienced difficult intubation. Of note, 20 patients in the study by Koh et al (52) and 11 in the study by Yentis et al (50) had difficult intubation despite a favorable modified Cormack-Lehane Grade, emphasizing that difficult intubation is also related to operator and resource variability. These variabilities limit one's ability to generalize the prevalence of difficult intubation to other populations. Since laryngoscopy grading is widely reported and difficult intubation is situationally dependent, Cormack-Lehane classification is likely a more uniform standard for predicting the difficult airway until a more consistent and reproducible comparator becomes available.

Another limitation of this study is that it did not analyze all the individual indices pooled together. However, as other studies have approached this (44, 45, 47, 48), such an analysis would likely again demonstrate that excessive heterogeneity between methods prevents any meaningful conclusions about airway ultrasound. This review suggests that a multiple assessment approach is potentially helpful. Based on the domain-specific analyses, a potential protocol could include an assessment of preepiglottal tissue thickness (TTD), hyomental distance assessed at a standard degree of patient neck extension (APD), and tongue thickness evaluated in the coronal plane with well-defined landmarks (OSD). A standardized approach to reporting is also necessary, as well as recommendations for the minimum capabilities of ultrasound equipment used in the assessment. The equipment recommendations optimally should consider the capabilities of machines likely found in clinical areas where intubation occurs. All studies in previously performed meta-analyses excluded patients with preexisting facial abnormalities and burns, which could lead to difficult laryngoscopy. Although patients with facial abnormalities and burns are not represented in the available literature, further study is warranted given the diagnostic challenges these patients face in determining whether they have a difficult airway in emergency settings.

CONCLUSIONS

Ultrasound measurements in three domains may serve as predictors for difficult laryngoscopy. The APD, which includes sonographic assessment of hyomental distance, may be more accurate than other domains. Despite low risk of overall bias in the available literature, studies are heterogeneous, and individual tests are likely inadequate. Deriving a composite assessment using multiple airway ultrasound tests is an area for further research and development.

ACKNOWLEDGMENTS

We appreciate the contribution of Dr. Guillaume Besch, MD, PhD, in providing valuable information for this investigation.

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All the authors helped conceptualize the article, perform the systematic review and meta-analysis of the literature, write and edit the final article.

Dr. Su received funding from Society of Critical Care Medicine, Children's Hospital of Philadelphia, the University of Texas Health Science Center, San Antonio, Stanford University, and Society for Pediatric Anesthesia. The remaining authors have disclosed that they do not have any potential conflicts of interest.

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